Standardizing MR image intensity in multi-centre studies

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Introduction

The standardization of the inter-subject intensities of MR images acquired with the same protocol is an important, but not a simple, task required by many analysis schemes. Its importance becomes even clearer once analysis is to be performed on data from large multi-centre trials, which often involve a variety of scanner manufacturers, field strengths and an inherent diversity of protocols. When the outcome of such trials is the comparison of the outcome of identical methods upon the data, then it is imperative that the starting points are the same. Methods such as intensity-based segmentation algorithms are inherently sensitive to variations in the intensity distribution. In existing methods, e.g. histogram matching [1,2], the shape of the histogram is not guaranteed to be preserved, making it difficult to compare histograms between normal and diseased brain volumes. With this in mind a new intensity standardization method is introduced where the shape of the histogram is preserved.

Method

A multi-stage approach is taken. First image artefacts such as RF inhomogenity, and intra-slice intensity variation in data acquired interleaved, are corrected. Then, samples from two of the three major tissue classes (e.g. grey-matter (GM), white-matter (WM) and CSF) within the modality to be corrected are required. To do this a simple pre-segmentation is needed, which is simplest to perform on a co-registered image from a modality with clearly defined classes e.g. a T1-weighted protocol. Conservative borders between the classes are found, and only the upper 80% of voxels within each thus-obtained class are then used as samples for the next stage. By obtaining such a robust, highly homogenous sample set, problems of partial-volume, non-brain, mixed class, and disease-induced distortions are suppressed. These samples are then used for the normalization stage. Here the mean and the standard deviation of two classes are determined, and then used to zero-mean the entire dataset, and to fix the standard deviation (std) at 1. Finally, in order to avoid any negative-valued voxels, a 'de-normalization' is applied where a new (arbitrary) mean and standard deviation are applied to the dataset. The values chosen have no effect upon the image appearance as the contrast-to-noise ratio (CNR) between tissue classes is maintained.

$$CNR_{AB} = 20 \cdot \log\left(\frac{|\mu_A - \mu_B|}{\sqrt{\frac{\sigma_A^2 \cdot N_A + \sigma_B^2 \cdot N_B}{N_A + N_B}}} \right) \quad [dB]$$

The CNR_{AB} is an image contrast measure based on the relative separation between two intensity distributions where μ_A is the mean intensity of tissue A, σ_A the standard deviation and N_A the number of voxels. Similarly for B.

Results

Over a three year period 487 brain volumes were scanned at 9 different centres in the European LADIS (Leukoraiosis And DISability) project with different protocols. Here the T1-weighted Magnetization-Prepared Gradient-Echo (MPRAGE) protocol was used for the validation due to its optimal tissue contrast. CSF and WM were used as primary tissue classes and the de-normalisation factors were set to mean=150 and std=15. The mean values from the three dominating tissue classes before and after normalization are shown in Figure 1. Beforehand, intensity variation is observed even within centres. The extremely large variation in centre 3 can be explained by the use of different scanners. After normalisation, the inter-subject and tissue variation are clearly standardized. The CNR between all three tissue classes remains unchanged ($p>0.96$, paired t-test), indicating that the images are visually identical post standardization. Outliers caused by incorrect protocol parameters are easy to isolate, e.g. in subject 151 and 155, GM and WM are overlapping indicating low initial image quality (prior $CNR_{GM\text{-}WM}$ -150dB and -220dB respectively), verified by visual inspection in Figure 2. Note that even in presence of erroneous images, the method performs correctly, and original CNR is maintained.

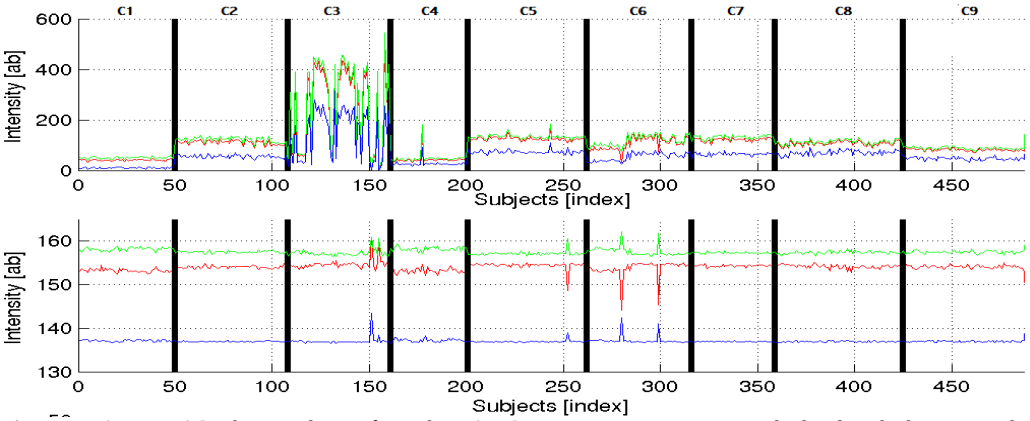

Figure 1 487 MPRAGE brain volumes from the LADIS project were intensity standardized with the proposed method. (y-axis) Mean intensity values of dominating tissues found by pre-segmentation of CSF (blue), GM (red), WM (green). (x-axis) Subjects divided into the 9 different centres (C1-C9). C3 used a 0.5 Tesla MR scanner, all others a 1.5 Tesla scanner. Top) Before and Bottom) after intensity standardization were tissues classes of all subjects are seen to be homogeneous.

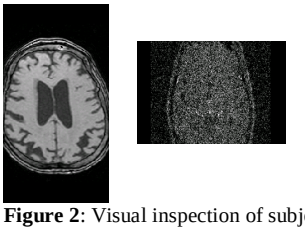

Figure 2: Visual inspection of subject 155 and 151 (right) before intensity normalisation. The low $CNR_{GM\text{-}WM}$ after normalisation can be explained by low prior image quality.

Conclusion

A new approach to intensity normalization has been developed. It overcomes the problems inherent in many other methods such as histogram-matching, because the shapes of the histograms are preserved. In addition, the CNR is maintained so there is no effect upon subjective rating. The result is the ability to perform identical pre- and post-processing, and analysis methods on all scans from different MR centres with no bias.

References

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2 Wang L, Lai HM, et al., Correction for variations in MRI scanner sensitivity in brain studies with histogram matching. MRM. 1998 Feb;39(2):322-7.